

Amendment Under 37 CFR §1.111  
Marco GENTILE et al.  
Serial No.: 08/894,733

Group Art Unit: 1614  
Examiner: Phyllis G. Spivack  
August 27, 1998

REMARKS

Claim 1 has been amended to recite the term "properties" in the plural and the transition phrase "comprising", as suggested in the Office Action. Other changes are the correction of the phrase "an inert gas atmosphere" and the recitation that the solution is being kept away from light. The recitation that the solution is being kept away from light is supported in the description, in particular page 6, line 13.

Claims 1-10 are under consideration in the present application. Claims 1-10 are directed to a pharmaceutical composition with anti-inflammatory and analgesic properties comprising an alkylammonium salt of a 2-arylpropionic acid selected from the group consisting of ketoprofen, ibuprofen, naproxen, tiaprofenic acid, with the following additional characteristics:

- osmolarity between 270 and 310 mOsm/kg;
- pH between 7.0 and 7.5;
- no preservatives or supporting substances;
- preparation and storage in an inert gas atmosphere and away from light.

Claim 1 was objected to in the Office Action because of minor informalities. Reconsideration and withdrawal of the objections is respectfully requested in view of the corrections to claim 1 as suggested in the Office Action.

Claims 1-10 were rejected under 35 U.S.C. §103(a) as obvious over Bosone et al. (WO 94/20449). Bosone is commonly assigned with the present application and names one inventor who is also named in the present application (Mr. Gaetano Clavenna). Bosone is cited in the

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International Search Report and also on page 6 of the specification of the present application. According to the Office Action, Bosone allegedly teaches the parenteral administration of compositions comprising ketoprofen in racemic and enantiomeric form with anti-inflammatory and analgesic properties. It is asserted in the Office Action that the application of the teaching in Bosone to the other compounds of the Markush group in claim 1 would have been obvious in view of the similarity in structure and pharmacological activity, and that the osmolarity, pH, absence of preservatives, and use of inert gas would have been an obvious selection of optimal conditions through routine experimentation.

The rejection is respectfully traversed for the following reasons.

It is submitted that the claimed compositions are not obvious because a person of ordinary skill in the art at the time the invention was made would have considered the presence of at least a preservative as necessary in compositions such as those suggested in Bosone. The only reference to pharmaceutical compositions in Bosone is a statement that "the salts of the invention may be suitably mixed with pharmaceutically acceptable excipients and formulated in a suitable manner for parenteral administration" (page 9, line 28 of Bosone). This description in Bosone clearly refers to a possible pharmaceutical composition formulated in a manner known in the art, with no novel characteristics except the active compound disclosed in Bosone. Thus, to a person of ordinary skill in the art at the time the present invention was made, the presence or absence of preservatives would not have been "parameters well within the purview of those skilled in the art" as alleged in the Office Action, because the addition of preservatives or co-solvents up to

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a quantity of about 2.5 % by weight is of usual and routine practice in parenteral formulations.

Moreover, the practice of adding a preservative would have been considered particularly necessary by a person of the art because the pharmaceutical compositions in Bosone contain active compounds which are known to undergo degradation. In support thereof, the Applicants submit copies of four journal articles documenting the photodegradation of active compounds such as those disclosed in Bosone. In view of the above, the suggestion in Bosone of compositions "formulated in a suitable manner for parenteral administration" would have been, for a person of ordinary skill, a teaching that the compositions must contain a preservative in order to avoid the degradation of the active compounds.

In contrast, an important improvement of the claimed compositions is that, in the absence of alcohols to solubilize the possible degradation products of ketoprofen compounds, the patients have a precise information about the quality of the composition. If the active principle in the composition is altered, the aspect of the composition is changed and the patient is advised of the alteration.

In further support of the above, a Declaration under Rule 1.132 by Mr. Clavenna, who is named as an inventor in Bosone and in the present application, is submitted concurrently herewith. The Declaration includes a report on comparative tests performed on a claimed composition without preservatives and the same compositions including preservatives. The test results in the Declaration show in particular the advantages of the claimed compositions without preservatives over compositions of the prior art containing preservatives as in Bosone, as

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presented above. In addition, the Declaration contains a statement by Mr. Clavenna to the effect that the teaching of "pharmaceutically acceptable excipients" in Bosone includes preservative substances.

In conclusion, the invention as claimed is not obvious over Bosone, and the invention as claimed is thus patentable. It is believed that the claims are in allowable condition and a notice to that effect is earnestly requested.

In the event there is, in the Examiner's opinion, any outstanding issue and such issue may be resolved by means of a telephone interview, the Examiner is respectfully requested to contact the undersigned attorney at the telephone number listed below.

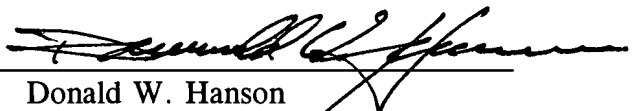
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In the event this paper is not considered to be timely filed, the Applicants hereby petition for an appropriate extension of the response period. Please charge the fee for such extension and any other fees which may be required to our Deposit Account No. 01-2340.

Respectfully submitted,

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Enclosures: Declaration under Rule 1.132 by Mr. Clavenna  
Journal of Photochemistry and Photobiology 104 (1997) 119-121;  
60 (1994) 96-101; 57 (1993) 486-490; 46 (1987) 991-996  
Photoderm. Photoimmun. Photomed. (1991) 8(5) 218-221  
Journal of Pharmaceutical Sciences 81 (1992) 181-182